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Recurrent post-partum seizures after epidural blood patch

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There are many causes for headaches after childbirth. Even though postdural puncture headache (PDPH) has to be considered in a woman with a history of difficult epidural anaesthesia, pre-eclampsia should always be excluded as an important differential diagnosis. We report a case with signs of late-onset pre-eclampsia where administration of an epidural blood patch (EBP) was associated with eclampsia. A hypothetical causal relationship between the EBP and seizures was discarded on the basis of evidence presented in this report.

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Headaches after childbirth do not necessarily reflect postdural puncture headache (PDPH), even with a history of a difficult epidural anaesthetic. As there are many causes for post-partum headaches, careful medical examination is warranted before giving an epidural blood patch (EBP) to a patient in whom conservative therapy for PDPH failed. Particularly, late onset pre-eclampsia should be excluded. We report a case where administration of an EBP for what was believed to be PDPH was associated with tonic-clonic seizures. Subsequent clinical and laboratory work-up was consistent with undiagnosed mild pre-eclampsia and eclampsia. A hypothetical causal relationship between

EBP and seizures was discarded on the basis of both clinical and published evidence.

Case report

A 34-yr-old primigravid healthy woman of Asian origin at 37 weeks' gestation requested epidural analgesia during active labour at 5 cm cervical dilatation. Her medical history was unremarkable, as was the course of pregnancy. Antenatally, arterial pressure was always within the normal range and on two occasions mild proteinuria was diagnosed. On admission, a low plasma albumin concentration of 25 g

litre⁻¹ (normal range 35–52 g litre⁻¹) was measured; platelet count and coagulation profile were within normal limits. There were no signs suggestive of pre-eclampsia or any neurological disorder.

Despite a normal body mass index (26.7 kg m⁻²), identification of the epidural space was difficult and only accomplished by a senior anaesthetist after several unsuccessful attempts by a trainee. The possibility of an accidental dural puncture could not be excluded, even though there was no evidence of cerebrospinal fluid (CSF) loss during placement of the needle or on aspiration. After a test dose of lidocaine 60 mg, epidural analgesia was established using bupivacaine 0.125%, 15 ml supplemented with epidural fentanyl 50 µg. Thereafter, an epidural infusion of bupivacaine 0.125% with fentanyl 0.001 mg ml⁻¹ at 10 ml h⁻¹ provided good pain relief throughout labour. Two hours after initiation of epidural analgesia, a healthy 2390 g boy was born, with Apgar scores of 7/9/9.

On the morning after delivery, about 7 h after initiation of epidural analgesia, the mother complained of headache, which was diagnosed as PDPH. It was associated with a left-sided hearing deficit and tinnitus. Initial conservative therapy consisted of oral caffeine 600 mg day⁻¹, oral diclofenac 150 mg day⁻¹, i.v. propacetamol 8 g day⁻¹ and Ringer's solution for supplementary i.v. hydration (2000 ml day⁻¹).

Because these symptoms persisted, an EBP was provided on the third day after delivery using 14 ml of autologous blood, which was injected without any technical difficulty into the epidural space. There was immediate and marked relief of headache. After an interval of approximately 2 h, the first episode of generalized tonic-clonic seizures was observed. About 1 h later, another episode of seizures occurred. At the outset of the seizures, the patient reported visual hallucinations that turned rapidly into progressive loss of vision followed by tonic and clonic jerking of the left leg that preceded generalized convulsions accompanied by loss of consciousness. The first and second fits were treated successfully with i.v. diazepam and clonazepam respectively. The patient was transferred temporarily to the medical intermediate care unit, where an arterial pressure of 140/97 mm Hg was recorded. The rise in systolic and diastolic arterial pressure was transient. In the medical intermediate care unit, uric acid concentrations increased for a short time (487 µmol litre⁻¹, normal range 173–359 µmol litre⁻¹) in association with a more consistent rise in liver enzymes (aspartate and alanine aminotransferases 84 and 111 U litre⁻¹ respectively, normal range 10–36 U litre⁻¹) and lactic dehydrogenase (323 U litre⁻¹, normal range 135–214 U litre⁻¹). Platelet count and coagulation profile were always within normal limits.

The neurological work-up performed after the seizures did not show any evidence for intracranial pathology or increased intracranial pressure. There was also no evidence of a focus responsible for acute cerebral dysfunction, such

as an expanding brain lesion or sinus vein thrombosis, on the basis of results from electroencephalography (EEG) and a cranial computed tomography (CT) scan including CT venography. Four days after the seizures, magnetic resonance imaging (MRI) did not reveal any evidence of intracranial lesions caused by cerebrovascular accidents or by infectious disease. In the absence of clinical and laboratory signs suggestive of meningitis, the neurological consultant did not perform a diagnostic lumbar puncture for fear of recurrence of her headache. He then suggested that seizures triggered by the EBP could not be dismissed as a differential diagnosis, at least as long as overt clinical and laboratory symptoms suggestive of pre-eclampsia and eclampsia or metabolic disturbances seemed to be missing.

The further clinical course was uneventful and the patient had recovered fully from the hearing deficit and the tinnitus when assessed by a consultant in otolaryngology during a follow-up examination on day 3 after the EBP. Because of her clinical condition, audiometry was postponed. She left hospital 7 days after delivery in good condition without any neurological deficit. Anticonvulsive therapy was not continued. One month later, during a follow-up assessment, she was in excellent condition and did not report any further seizures.

Discussion

PDPH is an intriguing clinical entity whenever it occurs. Although being clearly related to deliberate or inadvertent puncture of the dura, a variety of independent factors influence and modulate both the frequency and severity of its appearance.¹ Repeated dural punctures have been shown to increase the incidence of PDPH significantly.² Impairment in performing daily activities tends to persist as long as PDPH and related symptoms impinge upon the patient's well-being (median duration 4.6–6 days, range 1–10 days)³ and may delay discharge from hospital. If neglected, PDPH can result in chronic headache.^{4, 5} Effective treatment of PDPH is important because patients do not wish to remain bed-bound. In a patient survey, bed rest ranked as the second worst aspect of the PDPH experience.⁶

If conservative analgesic therapy for PDPH fails, administration of an autologous EBP is a highly effective therapeutic tool. According to a prospective observational study in a mixed population, the effectiveness of an EBP in completely relieving PDPH was as high as 75% (*n*=377), while incomplete relief of symptoms was observed in 18% (*n*=93) and therapeutic failure was noted in 7% (*n*=34).⁷ On the basis of these results, it is reasonable to consider whether an EBP should be offered as a prophylactic measure to anybody who is highly susceptible to the development of PDPH after a dural tap.⁸ A prophylactic EBP of autologous blood 17–20 ml injected via the epidural catheter was demonstrated to be effective in seven obstetric patients.⁹ Similarly, a prospective, sequentially randomized study

produced evidence for the effectiveness of a prophylactic EBP using autologous blood 15 ml given through the epidural catheter to 39 parturients; the incidence of PDPH was reduced to 21% compared with 80% in controls.¹⁰ However, only 35% of women serving as controls eventually received an EBP and 16% of those given a prophylactic EBP required a second EBP.¹⁰

Apart from the fact that blood patching within 48 h has been found to have a failure rate of 59% as opposed to 11% when delayed for more than 48 h,¹¹ an EBP by itself is not devoid of risks and complications. While the majority of side-effects, such as low back pain, neck stiffness and occasional radiating pain in the legs, are transient,¹² a minority of complications, such as aseptic meningeal irritation,¹³ radiculopathy¹⁴ and lumbosacral syndrome,¹⁵ may persist for weeks to months. Therefore, it is our practice to wait until PDPH develops. Such a policy is encouraged by reports indicating that even long-lasting PDPH can be treated successfully with an EBP.^{5 12 16}

In this patient, the presence of a headache completely unrelated to dural puncture or aggravated by PDPH has to be taken into account as subtle signs suggestive of mild pre-eclampsia were observed, a condition ultimately complicated by eclampsia. According to this hypothesis, the development of pre-eclampsia culminating in eclampsia was masked by headache of dual origin. This would be in line with current theories that challenge the classical picture of pre-eclampsia and eclampsia, as there is accruing evidence that 'seizures may precede hypertension or proteinuria. In other words, the term pre-eclampsia is misleading because eclampsia can precede pre-eclampsia'.¹⁷ For this very reason, occurrence of headache (50%), visual disturbances (19%) and epigastric pain (19%) become more important as premonitory signs heralding impending eclampsia in such individuals.¹⁷ Visual impairment has been shown to be related to cerebral or retinal vasospasm.^{18 19} In particular, an association of elevated cerebral perfusion pressure with headache has been observed in 88% of pre-eclamptic women.²⁰ In 1992, the incidence of eclampsia in the UK was found to be nearly one in 2000 pregnancies, with 44% occurring post partum.¹⁷ In the USA, the natural history of eclampsia was analysed retrospectively: six of 53 women (11%) with eclampsia had post-partum seizures and two of them convulsed as long as 5 days after delivery.²¹ Headache preceded seizures in 34 cases (64%) and visual disturbances in 16 cases (30%). Only a minority of women (13%) were diagnosed as having severe pre-eclampsia before seizures. Thus, the authors stated that 'eclampsia was not found to be a progression from severe pre-eclampsia. In 32 of 53 cases (60%) seizures were the first signs of pre-eclampsia'.²¹

A case history of a patient suffering from pregnancy-induced hypertension and PDPH has features common with the patient described in our report.²² Before the EBP with 10 ml of autologous blood on the third day post partum, she had received caffeine sodium benzoate 1000 mg i.v. over a

3 h period. Twenty minutes after the EBP was performed, the patient developed tonic-clonic seizures of approximately 30 s duration. Despite i.v. administration of diazepam and magnesium sulphate, two additional seizures occurred 20 min later. Neurological examination, CT scan and EEG were normal. The authors discarded caffeine as a potential cause of seizures because caffeine toxicity would preferentially produce transient dizziness rather than convulsions. In contrast, they referred to some studies indicating that caffeine might reduce seizure threshold and thus unmask an underlying seizure disorder, such as pre-eclampsia. Hence, late post-partum eclampsia was considered the most plausible aetiology.²²

Because there is no strong evidence linking EBP with seizures in the absence of pre-eclampsia, other aetiologies have to be considered in the differential diagnosis. Eight cases of new-onset generalized seizures occurring 2–7 days after spinal anaesthesia were retrieved from a database including more than 100 000 pregnancies; they all had PDPH associated with visual disturbances, progressing to cortical blindness in three patients.²³ A moderate and transient increase in arterial pressure, observed in half of the patients after the seizures, was interpreted as a non-specific haemodynamic response to generalized convulsions and not as pre-eclampsia. All of these women underwent diagnostic lumbar puncture that failed to identify a specific cause for the seizures. However, signs of cerebral vasospasm and evidence of regional blood flow changes were found in three women (angiography). CT scans were normal in all eight women, as was EEG ($n=7$) and MRI ($n=5$). In one of these women, an EBP was performed without any dire effects 5 days after the seizure. The authors concluded that changes in cerebral vascular reactivity during severe PDPH might trigger seizures without the presence of further pathology.²³ According to another report, a PDPH that was complicated by brief seizures on the third day after delivery was treated successfully with an EBP.²⁴ In that case, neuroradiological investigations were not conclusive for a minor intracranial haemorrhage suspected because of slightly bloodstained CSF.

The chronological association of EBP and seizures led to speculation regarding the possible role of blood administration in triggering seizures.²⁵ The presence of discrete and unspecific EEG changes consistent with a postictal state led to the hypothesis that the seizures had their origin in the spread of blood into the subarachnoid space.

What are the arguments for and against this hypothesis and what is the evidence in the literature? Because MRI is sensitive to the paramagnetic effect of iron within the haemoglobin molecule, it should provide evidence of blood within the subarachnoid space.¹⁴ In fact, a spinal subdural haematoma was diagnosed using MRI in a patient who developed cauda equina syndrome and severe and persistent back pain after a total of six EBPs to treat PDPH after repetitive epidural phenol injections for chronic pain.¹⁴ Although most of an EBP will be found in the epidural space, where an 18 ml volume of blood was observed to

spread over four spinal segments and to extend through the neural outlet foramina, MRI signals from the CSF suggested that a small proportion of blood entered the subarachnoid space as it reached the paravertebral space.^{26, 27} Spread of blood into the CSF was not associated with any neurological side-effects in a patient who suffered from PDPH after a dural tap with a Tuohy needle.²⁶ Blood does not exert a physiological effect in the subarachnoid space and is rapidly cleared from the CSF by the arachnoid villi, and neither blood nor its breakdown products have been shown to be relevant in the aetiology of aseptic arachnoiditis.²⁸ Such an assumption was corroborated by early experience of 'subdural' (subarachnoid) blood patching with no evidence of neurological sequelae in 100 consecutive patients.²⁹ These patients received one-third of 2.5 ml of autologous blood after injection of tetracaine for spinal anaesthesia, then, 'as the needle was withdrawn slowly, the remainder of the clot was injected in a manner attempting to plug the hole itself and to deposit some clot in the epidural space at the puncture site'. The authors reported a zero incidence of PDPH in the group receiving blood, compared with a 15% incidence in the control group. Arachnoiditis or aseptic meningitis as a result of an EBP has, with one exception, not been reported.¹³ In that case, an EBP performed in the presence of low-grade fever led to subsequent short-term exacerbation of a febrile condition associated with signs suggestive of acute meningitis that, with antibiotics, subsided within 24 h. Neither focal neurological signs nor seizure activity was present.

In conclusion, particular attention should be directed to post-partum women presenting with headache that is thought to be caused by inadvertent dural puncture. Even in the case of a dural tap followed by PDPH, pre-eclampsia should always be excluded as an important differential diagnosis.

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